

Oct. 7, 1999

MEMORANDUM

SUBJECT: **Thiabendazole** (060101) Reregistration Case No. 2670. Anticipated Residue Assessment for the HED Risk Assessment. DP Barcode D259731.

FROM: Thurston G. Morton, Chemist
Reregistration Branch 4
Health Effects Division (7509C)

THROUGH: Susan V. Hummel, Branch Senior Scientist
Reregistration Branch 4
Health Effects Division (7509C)

TO: Beth Edwards/William Sproat, PM#51
Reregistration Branch
Special Review & Reregistration Division (7508W)

Anticipated residues were generated for the chemical thiabendazole for use in acute and chronic dietary exposure assessments. Thiabendazole [2-(4-thiazolyl)benzimidazole] is a systemic fungicide and is currently registered for food/feed uses on a variety of field, fruit, and vegetable crops. Thiabendazole may be applied as a pre-plant application (potato seed piece) or post-harvest application as a spray, dip, or wax. Tolerances for residues of thiabendazole *per se* in/on plant raw agricultural commodities (RACs) and processed plant commodities have been established under 40 CFR§180.242(a). Tolerances have also been established for the combined residues of thiabendazole *per se* and its metabolite, 5-hydroxy-thiabendazole, in milk at 0.4 ppm and in eggs, meat, meat-by-products (mbyp), and fat of livestock at 0.1 ppm [40 CFR§180.242(b)]. Residues of concern in plants include thiabendazole *per se* and its metabolite benzimidazole (free and conjugated)(L. Cheng, 3/11/92). The HED Metabolism Committee (L. Cheng, 2/14/92) concluded that thiabendazole residues to be regulated in animal commodities will include thiabendazole *per se*, 5-hydroxy-thiabendazole (free and conjugated), and benzimidazole. Anticipated residues were generated for only those food uses which the HED Residue Chemistry Chapter (J. Garbus, 10/99) reassessed. Tolerances for several food uses (avocado, mango, papaya, cantaloupe, soybean, and strawberry) were recommended for revocation due to insufficient residue data. Tolerance level residues will be used in the dietary exposure analyses for these food forms.

			PB	Juice/Juice concentrate	44NZ, 464@0.021, 169Z	NA	0.026
Limes/10	48	PDP (Oranges)	NB	Peeled fruit-uncooked, cooked	1000NZ, 405@0.032, 1522Z	NA	0.156
			PB	Peel/, Peeled fruit-canned	641NZ, 259@0.032, 975Z	NA	0.156
			PB	Juice/Juice concentrate	44NZ, 464@0.021, 550Z	NA	0.026
Grapefruit/10	45	PDP (Oranges)	NB	Peeled fruit-uncooked, cooked	1000NZ, 405@0.032, 1717Z	NA	0.156
			PB	Peel/, Peeled fruit-canned	641NZ, 259@0.032, 1100Z	NA	0.156
			PB	Juice/Juice concentrate	44NZ, 464@0.021, 621Z	NA	0.026
Lemons/10	5	PDP (Oranges)	NB	Peeled fruit-uncooked, cooked	1000NZ, 405@0.032, 26695Z	NA	0.156
			PB	Peel/, Peeled fruit-canned	641NZ, 259@0.032, 17100Z	NA	0.156
			PB	Juice/Juice concentrate	44NZ, 464@0.021, 9652Z	NA	0.026
Potatoes/10	50	PDP	NB	White-peeled and white-whole: uncooked, cooked, baked, boiled, fried; white-peel only	1000NZ, 4435@0.028, 5435Z	NA	0.159
			PB	White-peeled and white-whole: canned, frozen	130NZ, 224@0.028, 353Z	NA	0.159
			B	White-dry	NA	0.159	0.159
Mushrooms/40		FT	PB	All food forms	6NZ	NA	16.0
Sweet Potatoes/0.05	25	PDP	PB	Canned	4NZ, 297@0.015, 901Z	NA	0.016
			NB	Cooked, baked, boiled, fried	4NZ, 297@0.015, 901Z	NA	0.016

Wheat/0.2	1%	1%	PDP	B	All food forms	NA	0.019	0.019
Goat Kidney, Goat Meat byproducts, Goat other organ meats, Sheep Kidney, Sheep Meat byproducts, Sheep other organ meats, Beef & Veal Meat byproducts, Beef & Veal other organ meats, Beef & Veal kidney/0.4		50%	FT	NB	All food forms	1NZ, 1Z	NA	0.068
Goat Liver, Sheep Liver, Beef & Veal liver/0.4		50%	FT	NB	All food forms	1NZ, 1Z	NA	0.034
Pork meat byproducts/ Pork other organ meats/Pork Kidney/0.4		50%	FT	NB	All food forms	1NZ, 1Z	NA	0.01
Pork Liver/0.4		50%	FT	NB	All food forms	1NZ, 1Z	NA	0.004
Milk/0.1		50%	PDP	PB	All food forms	6NZ, 534@0.008, 539Z	NA	0.008

Detailed Discussion:

Fruit and vegetable PDP data (1995-1997) analyzed for thiabendazole only. Given that post-harvest applications result in the highest potential thiabendazole residues in/on raw agricultural commodities, HED concluded that residues of benzimidazole (free and conjugated) are unlikely to contribute significantly to the total thiabendazole residues (S. Mason, D207850/D214188, 1/99). Therefore, PDP data for all commodities except wheat could be used directly. A factor of 1.8 to convert the PDP data to account for benzimidazole residues in wheat grain was calculated from the nature of the residue study in wheat (L. Cheng, D165718, 3/11/92). Milk PDP data was analyzed for thiabendazole and 5-hydroxy-thiabendazole. Residues of benzimidazole were not detected in milk in the metabolism study (L. Cheng, D170818, 3/2/92). Therefore, PDP data was used for acute and chronic dietary exposure analyses.

Pome Fruits

Registered labels permit application to pome fruits as a post-harvest dip, flood, or spray at a maximum single application rate of 0.48 lb ai/100 gallons. Two applications per season are allowed for apples and one application per season for pears. Maximum treatment time is 3 minutes. Apples may be treated before and after storage. The BEAD maximum percent crop treated estimates indicate 62 % CT for apples and 90 % for pears. Apple processing studies have been found to be adequate (S. Mason, 1/8/99, D207850). The processing factors for thiabendazole residues in were 0.28X in apple juice, 3.6X in apple wet pomace, and 12.1X in apple dry pomace. Adjustment factor 1 in DEEM[®] for pome fruit juices was set to 1 and the factor for pome fruit juice concentrates was adjusted accordingly to preserve the ratio between juice and juice concentrate in DEEM[®].

Extensive PDP data are available for apples, pears, and apple juice. Apple monitoring data was translated to other pome fruits except pears. Apple juice was translated to pear juice. The PDP monitoring data was used to generate residue distribution files (RDFs) for the acute probabilistic analysis (non-blended and partially blended food forms), average residues for the acute analysis (blended food forms), and average residues for the chronic analysis (all food forms). Apple food forms include non-blended (uncooked, cooked, baked, boiled, and fried), partially blended (juice, canned), and blended (dried apples) food forms. For non-blended food forms (NB), single unit residue values were included in the RDF; these single unit residues were generated by way of decomposition of composite PDP residue values using the method described in the H. Allender paper (5/26/99) titled "Statistical Methods for Use of Composite Data in Acute Dietary Risk Assessment." The number of zeroes and ½ LODs were adjusted accordingly to preserve the % detects found in the original PDP data and to account for the % crop treated. These numbers were then added into the appropriate RDF and also entered into Table 1. For partially blended food forms (PB), the PDP residue distribution was directly incorporated into the RDF with no decomposition. For blended food forms (B), the average of composite PDP monitoring data was used as a single point estimate. There were 1194 samples of apples with 721 detects, 854 apple juice samples with 281 detects, and 695 samples of pears with 467 detects. Apple juice was translated to pear juice.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Apples	721/1194	60.4	0.036	617.157
Apple Juice	281/854	32.9	0.017	56.815
Pears	467/695	67.2	0.016	261.177

Banana and Plantain

Registered labels permit application to bananas and plantains as a post-harvest spray until runoff at a maximum single application rate of 0.08 lb ai/26.4 gallons. One application per season is allowed. BEAD estimates indicate a 50 % crop treated for bananas.

Extensive PDP data are available for bananas which was translated to plantains. Banana non-blended food forms include uncooked, cooked, baked, boiled, and fried. Partially blended food forms include canned and juice. Blended food forms include dried bananas. For non-blended food forms (NB), single unit residue values were included in the RDF; these single unit residues were generated by way of decomposition of composite PDP residue values. For partially blended food forms (PB), the PDP residue distribution was directly incorporated into the RDF with no decomposition. For blended food forms (B), the average of composite PDP monitoring data was used as a single point estimate. There were 486 samples of bananas with 251 detects.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Banana	251/486	51.6	0.015	21.684

Carrots

Registered labels permit application to carrots as a post-harvest dip at a maximum application rate of 1.25 lb ai/100 gallons. One application per season is allowed and maximum treatment time is 10 minutes. BEAD estimates indicate a maximum of 1 % crop treated for carrots.

Extensive PDP data are available for carrots. Carrot non-blended food forms include uncooked, cooked, baked, and boiled. Carrot partially blended food forms include canned and frozen carrots. For non-blended (NB) and partially blended food forms (PB), the PDP residue distribution was directly incorporated into the RDF with no decomposition because only one residue detection was found. There were 1193 samples of carrots with 1 detect.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
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Carrot	1/1193	0.08	0.024	0.05
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Citrus

Registered labels permit application to citrus as a sequential post-harvest aqueous dip and wax at a maximum single application rate of 5000 ppm (1 gal. wax/3500 lb fruit). Two applications per season are allowed. Thiabendazole is first applied as an aqueous dip at up to 1000 ppm for up to 3 minutes prior to de-greening, followed by a second application (after de-greening and washing) of thiabendazole at up to 3500 ppm in wax. In AZ and CA, only a single post-harvest application is allowed as an application of thiabendazole in wax at up to 5000 ppm. The BEAD percent crop treated estimates indicate a % crop treated of 75 % CT for oranges, 48 % for limes, 45 % for grapefruit, and 5 % CT for lemons

Extensive PDP data are available for oranges and orange juice, which were translated to other citrus fruits. Adjustment factor 1 in DEEM[®] for citrus juices was set to 1 and the factor for citrus juice concentrates was adjusted accordingly to preserve the ratio between juice and juice concentrate in DEEM[®]. Citrus non-blended food forms include peeled fruit-uncooked and cooked. Citrus partially blended food forms include peel-all food forms, peeled fruit-canned, juice, and juice concentrate. There were 1201 samples of oranges with 641 detects and 677 samples of orange juice with 44 detects.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Oranges	641/1201	53.4	0.032	132.023
Orange Juice	44/677	6.5	0.021	3.349

Potatoes

Registered labels permit application to potato seed tubers prior to cutting or as a post-harvest mist application at a maximum single application rate of 0.0125 lb ai/2000 lb tubers. Two applications as a post-harvest mist application may be made per season and one application as a seed tuber treatment before cutting may be made. The BEAD percent crop treated estimates indicate 50 % CT for potatoes.

Extensive PDP data are available for potatoes. Potato non-blended food forms include white-peeled uncooked, cooked, baked, boiled, fried; white-whole uncooked, cooked, baked, boiled, fried; and white-peel only (all food forms). Potato partially blended food forms include white-peeled canned, frozen; and white-whole canned, frozen. Potato blended food forms include white-dry. The processing factor to be used for the food form potatoes/white-dry is 0.09X (J. Abbotts, D189323, 8/3/93). There were 707 samples of potatoes with 130 detects.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Potato	130/707	18.4	0.028	49.853

Mushrooms

Registered labels permit application to mushrooms either as a direct spray or in irrigation water at casing, fuzzing, pinning, and between breaks at a maximum single application rate of 0.24 lb ai/1000 ft². Four applications per season are allowed and a 12 hour PHI is specified. The label specifies that a maximum of 0.6 lb ai/1000 ft² or 0.48 lb ai/1000 ft² may be applied to each crop using irrigation water or direct spray (hand-sprayer) applications, respectively. BEAD did not submit an estimate of the % crop treated for mushrooms.

HED concluded that field trial data reflecting the registered use on mushrooms would be acceptable provided adequate storage stability data was submitted (D. Miller, 11/22/93, D186572). Merck and Co. submitted storage stability data and HED found this data to be adequate (S. Mason, 1/12/99, D214188). Fifteen field trial residue values were used in the residue distribution file (RDF) for mushroom and 100 % CT was used due to the fact that BEAD did not submit %CT estimates for mushrooms. All mushroom food forms are partially blended, therefore, the entire distribution of the field trial data was incorporated into a residue distribution file (RDF) for the acute Monte Carlo analysis. The average of the 6 field trial residue values were used in the chronic analyses.

Sweet Potatoes

Registered labels permit application to sweet potatoes as a pre-planting dip to seed roots at a maximum single application rate of 0.24 lb ai/7.5 gallons. One application per season is permitted and seed roots may be treated for a maximum of 10 minutes.

Extensive PDP data are available for sweet potatoes. Non-blended food forms of sweet potatoes include cooked, baked, boiled, and fried. Partially blended food forms of sweet potatoes include canned food forms. There were 1202 samples of sweet potatoes with 4 detects. The BEAD percent crop treated estimates indicate 25 % CT for sweet potatoes.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Sweet Potato	4/1202	0.3	0.015	0.257

Wheat

Registered labels permit application to wheat as a seed treatment.

Extensive PDP data are available for wheat. All food forms of wheat are considered blended therefore, an average residue was calculated from the PDP data. The BEAD percent crop treated estimates indicate an average/maximum of <1/<1 % CT for wheat. HED assumes a minimum of 1 % CT for inclusion into the dietary analysis. There were 631 samples of wheat with 3 detect. Thiabendazole did not concentrate in processed fractions of wheat (L. Cheng, 7/28/93, D190451).

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Wheat	3/631	0.5	0.006	0.093

Meat, Milk, Poultry, and Eggs

Extensive PDP data are available for milk. All food forms are considered partially blended. There were 1079 samples of milk tested with 6 detects. There is no reasonable expectation of finding quantifiable thiabendazole residues in poultry tissues and eggs resulting from the feeding of thiabendazole treated crops to poultry. There is no reasonable expectation of finding quantifiable thiabendazole residues in meat and fat of cattle, goats, horses, and sheep (J. Garbus, 10/99). Thiabendazole is also registered as an animal drug by FDA. FDA has established a tolerance for negligible residues of thiabendazole in uncooked edible tissues of cattle, goats, sheep, pheasants, and swine at 0.1 ppm. Therefore for the dietary analysis, 0.05 ppm (½ LOD) will be used for the meat of cattle, goats, sheep, horses, poultry, and swine. Anticipated residues were calculated for liver, kidney, and meat-by-products for cattle, goats, horses, and sheep. Anticipated residues were also calculated for milk. The anticipated residues were calculated using the thiabendazole and 5-hydroxy thiabendazole residues from the ruminant feeding studies (MRID 40789817) and either an acute maximum reasonable dietary burden (Table 2) or an chronic average reasonable dietary burden (Table 5). Benzimidazole residues were calculated using the ratio of benzimidazole to 5-hydroxy thiabendazole in the goat metabolism study (0.7X for liver and 0.6X for kidney) (L. Cheng, D170818/D169697, 3/2/92). The dietary burdens are listed in the following tables.

RAC	#Detects/#Sampled	% Detects	½ LOD (ppm)	Total of Detects (ppm)
Milk	6/1079	0.6	0.008	0.3

Table 2. Thiabendazole Acute Maximum Realistic Dietary Burden

Feed Commodity	% Dry Matter	% Diet	Anticipated Residue (HAFT) ppm	Dietary Contribution (ppm)

Beef Cattle				
Potato culls	20	40	7.3	14.60
Wheat grain	89	50	0.15	0.08
Wheat straw	88	10	0.23	0.03
Total				14.71
Dairy Cattle				
Potato culls	20	40	7.3	14.60
Wheat grain	89	40	0.15	0.07
Wheat straw	88	10	0.23	0.03
Wheat AGF	85	10	0.05	
Total				14.70
Poultry				
Wheat grain	NA	80	0.15	0.12
Wheat milled by products	NA	20	0.10	0.02
Total				0.14
Swine				
Potato culls	NA	50	7.3	3.65
Wheat grain	NA	50	0.15	0.08
Total				3.73

Table 3. Cattle Acute Anticipated Residues.

Tissue	25 ppm Feeding Level (1.7X)	75 ppm Feeding Level (5.1X)	250 ppm Feeding Level (17X)	Cattle Acute AR
Kidney	0.09/1.7=0.053	0.687/5.1=0.135	0.904/17=0.053	0.080 ppm ^a
Liver	0.07/1.7=0.041	0.28/5.1=0.055	0.345/17=0.020	0.039 ppm

^aUse for kidney, meat byproducts, and other organ meats for beef, goat, sheep, and veal.

Table 4. Swine Acute Anticipated Residues based on residue data from the ruminant feeding study.

Tissue	25 ppm Feeding Level (6.7X)	75 ppm Feeding Level (20X)	250 ppm Feeding Level (67X)	Swine Acute AR
Kidney	0.09/6.7=0.013	0.687/20=0.035	0.904/67=0.013	0.020 ppm ^b
Liver	0.07/6.7=0.010	0.28/20=0.014	0.345/67=0.005	0.010 ppm

^bUse for kidney, meat byproducts, and other organ meats for pork.

Table 5. Thiabendazole Chronic Average Realistic Dietary Burden

Feed Commodity	% Dry Matter	% Diet	Anticipated Residue ppm	Dietary Contribution (ppm)
Beef Cattle				
Potato culls	20	30	4.1	6.15
Wheat grain	89	50	0.05	0.03
Wheat straw	88	10	0.079	0.01
Wheat AGF	85	10	0.05	0.01
Total				6.20
Dairy Cattle				
Potato culls	20	30	4.1	6.15
Wheat grain	89	40	0.05	0.02
Wheat straw	88	10	0.079	0.01
Wheat AGF	85	20	0.05	0.01
Total				6.19
Poultry				
Wheat grain	NA	80	0.05	0.04
Wheat milled by products	NA	20	0.05	0.01
Total				0.05
Swine				
Potato culls	NA	20	4.1	0.82
Wheat grain	NA	80	0.05	0.04
Total				0.86

Table 6. Cattle Chronic Anticipated Residues.

Tissue	25 ppm Feeding Level (4X)	75 ppm Feeding Level (12X)	250 ppm Feeding Level (40X)	Cattle Chronic AR
Kidney	$0.09/4=0.023$	$0.687/12=0.057$	$0.904/40=0.023$	0.034 ppm ^c
Liver	$0.07/4=0.018$	$0.28/12=0.023$	$0.345/40=0.009$	0.017 ppm

^cUse for kidney, meat byproducts, and other organ meats for beef, goat, sheep, and veal.

Table 7. Swine Chronic Anticipated Residues based on residue data from the ruminant feeding study.

Tissue	25 ppm Feeding Level (29X)	75 ppm Feeding Level (87X)	250 ppm Feeding Level (290X)	Swine Chronic AR
Kidney	$0.09/29=0.003$	$0.687/87=0.008$	$0.904/290=0.003$	0.005 ppm ^d
Liver	$0.07/29=0.002$	$0.28/87=0.003$	$0.345/290=0.001$	0.002 ppm

^dUse for kidney, meat byproducts, and other organ meats for pork.

cc: Chem F, Chron F. Morton

RDI:ChemSAC: 9/22/99; SVH:10/7/99

TM, Thurston Morton, Rm. 816D CM2, 305-6691, mail code 7509